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Barbara Cuddon
REC Manager
Health Research Authority
Skipton House, 80 London Road, London SE1 6LH

Dear Barbara,

Re: Study Title: Randomized, Embedded, Multi-factorial, Adaptive Platform Trial for community - Acquired Pneumonia
REC reference: 18/lo/0660
EudraCT number: 2015-002340-14
IRAS project ID: 237150

Substantial amendment 15 (AM015) Expedited Approval

I am submitting substantial amendment AM015 for the REMAP-CAP study, I have made the below changes to the MHRA CTA.

Because i have made changes to the patient population i thought it best to submit to regulatory, ethical and competent authorities.

Changes to the MHRA CTA

1. Doses of Anakinra approved as per AM011, but not updated on the CTA.

Old dosing from Immune modulation domain v1:

300 mg of anakinra will be administered as an intravenous bolus injection via a central or peripheral line once daily. In patients with creatinine clearance of less than 30 ml/min or receiving renal replacement therapy, anakinra will be dosed only on alternate days.

Duration of therapy

Anakinra will be administered once daily until the patient has been breathing without receiving invasive mechanical ventilation for more than 24 hours or for 14 days in patients who continue to receive invasive mechanical ventilation.

New dosing from Immune modulation domain v2:

Anakinra will be administered as an intravenous bolus injection via a central or peripheral line. A loading dose of 300 mg will be administered, followed by maintenance doses of 100

mg of anakinra administered every 6 hours. In patients with creatinine clearance of less than 30 ml/min or receiving renal replacement therapy, anakinra will be dosed every 12 hours.

Duration of therapy

Anakinra will be administered four times daily until the patient has been breathing without receiving invasive mechanical ventilation for more than 24 hours or for 14 days in patients who continue to receive invasive mechanical ventilation. For patients not receiving invasive mechanical ventilation, the drug will stop on ICU discharge or after 14 days, whichever occurs first.

2. Correction to an error in our original MHRA CTA application regarding specific populations of patient included in this study. We had ticked excluding women of child bearing age (using and not using contraception) , but as discussed with the MHRA at that time, these patients would be included for some IMPs but not others. In light of the pandemic we feel this population of patients as well as pregnant women and breastfeeding women, would benefit from this study and would like to ensure they are able to be included. Pregnant and breastfeeding women are excluded from certain domains and if treating clinicians feel it would not be in their best interest to enter the study, they can be excluded on an individual basis

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